

June 9, 1949.

Dr. F. Moewus,
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Dear Dr. Moewus:

p11
I enclose reprints of a review article and of some of my experimental work which may be of interest to you. If I may apologize for the hasty treatment which was given to the genetics of the algae, it would be partly based on the difficulty of obtaining here a comprehensive and definitive set of your publications.

I would appreciate it greatly, therefore, if you could send me such of your works as are available still, and would place my name on your mailing list, a favor which I shall be glad to reciprocate.

Yours sincerely,


Joshua Lederberg,
Assistant Professor of Genetics.

mycelia from zygosporangia heterozygous for three factors. No sporangium yielded more than four mutually complementary sporangiospores, although all of the eight possible classes were recovered from several zygosporangia together. In dihybrid crosses, approximately equal numbers of *tetratype* and *ditype* zygosporangia were obtained, contrary to his own cytological findings, only a single nucleus contributes to the germ mycelium.

Zygosporangia of *Mucor mucedo* were subjected to a similar analysis by Emerson (1935), who concluded that only a single reduced nucleus is formed since no genetic diversity was found among the issue of a sporangium.

The non-disjunction of sex-incompatibility factors has been accounted for by Burgeff (1915). While he could account for this in some sporangium cultures by heterokaryosis for incompatibility factors, he was unable to segregate out the components except from the zygosporangia they produced. He concluded, therefore, that these mycelia contained unreduced nuclei heterozygous for the sex alleles. If these mycelia are diploid, they provide excellent material for the comparison of interactions within and across nuclear membranes.

Mucor grandis shows another sort of anomalous behaviour (1942b). The species is homothallic and produces superficially unreduced sporangia in pure culture. However, no cytological evidence was found either of nuclear fusion or of meiosis.

The utility of genetic analysis in the solution of life-cycle problems is illustrated by Emerson's work on *Allomyces* (1941). The species *pusillus* and *javanicus* differ primarily in the arrangement of gametangia. Although homothallic, the organisms can be separated by the separation of male and female gametangia. By following when segregation of the differential characters occurred, the order of reduction-divisions could be placed. It was shown that in *Allomyces* an alteration of diploid and haploid thalli "a most unusual affair; extensively developed thalli with true, actively dividing diploid nuclei are probably not ordinarily formed by any other mycelium."

Other fungi exhibit a wide range of nuclear and life-cycle problems, the potentialities of which have scarcely begun to be explored. Aside from the studies already alluded to on the Mucorales, *Allomyces*, and incidental observations on some Myxothallophyta (Emerson, 1935), there has been no consideration of these forms as subjects for genetic study, although it is almost certain that it would be of fundamental importance.

(ii) Algae

Work on algae has been overshadowed by the numerous studies of F. Moewus (cf. Buzzati-Traverso, 1947, p. 38) on the green alga *Chlamydomonas reinhardtii*. Unfortunately, this "most remarkable series of

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studies in biochemical genetics . . .” (Beadle, 1945*a*) has been challenged in almost every detail (Smith, 1946; Sonneborn, 1941; Lwoff, 1947). To these comprehensive analyses, the present writer can add no informed comment. However, earlier work on algæ should not be overlooked, and Hartmann’s review (1929) will be useful in planning experiments on this group.

Genetic recombination in bacteria and viruses will be dealt with separately because of the unique argument that must be used for its demonstration.

MODES OF GENETIC VARIATION

(i) *The Particulate Basis*

Genetic investigations of “perfect fungi” have clearly shown Mendelian corpuscular behaviour of genetic determinants; but there have been many attempts to formulate alternative systems for organisms, such as bacteria, less amenable to recombination analysis. Huxley wrote, speculatively, of bacteria that “the entire organism appears to function both as soma and germ plasm and evolution must be a matter of alteration in the reaction system as a whole” (1942). Similarly, Darlington (1939) refers to “genes which are still undifferentiated in viruses and bacteria.” However, these statements are now probably convenient targets for controversy rather than expressions of their authors’ present opinions.

The lack of outward differentiation of bacteria and viruses does give the appearance of holo-cellular propagation, and of an identity between direct transmission and inheritance. In binary fission, the substance of the cell is of course transmitted intact to the offspring. Inherited characters are fashioned out of this material. Rather than postulate an autonomous regulatory mechanism, therefore, many students have formulated the genetic system as the direct transmission of the material characters. Hinshelwood (1946), for example, has defined the bacterial cell as an extended fabric of enzymes with both auto- and hetero-catalytic properties. However, his admission that radiation induced mutations affecting enzymatic activity imply definite localisation of autocatalytic functions is difficult to distinguish from the abandonment of his definition.

The direct transmission theory may be disproved in several ways. First, bacteria are not so undifferentiated after all. In *Salmonella*, for example, they carry on their surfaces flagella containing serologically distinctive substances. When grown on agar containing phenol, they lose both flagella and specific antigens. A passage through ordinary medium suffices to restore these differentiated structures in their original form. The determinants of flagellar specificity are therefore transmitted in the absence of the flagella. The contrary result of a similar experiment, the inordinate delay in the restitution of antigens removed from the surface of *Paramecium aurelia* by antiserum